--IN THE CLAIMS--

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of claims

1.(amended) A method for drug discovery, said method comprising: (A) constructing one or more protein-fragment complementation assays (PCAs'); (B) testing the effects of chemical compounds on the activity of said assay(s); (C) using the results of said assay(s) to identify chemical compounds with desired activities with the proviso that said protein complementation assays do not utilize ubiquitin fragments and said assays are not two hybrid assays.

2.(amended) A method of screening chemical compounds, said method comprising: (A) constructing protein-fragment complementation assays for one or more steps in a cellular pathway; (B) testing the effects of said compounds on the activity of said assay(s); (C) using the results of said screen to identify compounds that activate or inhibit the cellular pathway(s) of interest with the proviso that said protein complementation assays do not utilize ubiquitin fragments and said assays are not two hybrid assays.

3.(amended) A method of screening chemical compounds, said method comprising: (A) selecting a chemical library; (B) constructing one or more protein-fragment complementation assay(s); (C) testing the effects of chemical compounds from said library on said assay(s); (C)

using the results of said screen to identify specific compounds that increase or decrease the signal generated in said assay(s) with the proviso that said protein complementation assays do not utilize ubiquitin fragments and said assays are not two hybrid assays.

4.(amended) A method of screening chemical compounds, said method comprising: (A) selecting a chemical library; (B) constructing one or more protein-fragment complementation assay(s); (C) testing the effects of chemical compounds from said library on said assay(s); (C) using the results of said screen to identify specific compounds which alter the subcellular location of the signal generated in said assay(s) with the proviso that said protein complementation assays do not utilize ubiquitin fragments and said assays are not two hybrid assays.

5. (amended) A method for constructing an assay, said method comprising: (a) selecting genes encoding proteins that interact; (b) selecting an appropriate protein reporter molecule; (c) effecting fragmentation of said protein reporter molecule such that said fragmentation results in reversible loss of reporter function; (d) fusing or attaching fragments of said protein reporter molecule separately to other molecules; (e) reassociating said protein reporter fragments through interactions of the molecules that are fused or attached to said protein fragments; and (f) measuring the activity of said protein reporter molecule with automated instrumentation with the proviso that said protein fragments are not ubiquitin fragments and said assay is not a two hybrid assay.

6.(amended) A method according to claim 5 whereby the protein reporter molecule is selected from the group consisting of an enzyme, a fluorescent protein, a luminescent protein, ~~a phosphorescent protein,~~ a monomeric protein, an antigen, or an antibody.

7.(amended) A method according to claims 1, 2, 3, 4, 5 or 6 whereby the protein reporter fragments are created by oligonucleotide synthesis, by fragmenting an intact reporter molecule, or by DNA amplification of a template.

8.(original) A method according to claim 1 wherein an optically detectable signal is generated in the assay.

9.(amended) A method according to claim 1 wherein the signal generated in the assay is fluorescence, bioluminescence, chemiluminescence~~, or phosphorescence.~~

10.(original) A method according to claim 1 whereby the assay is performed in multiwell formats, in microtiter plates, in multispot formats, or in arrays.

11. (original) A method according to claim 1, 2, 3, 4, 5 or 6 whereby the assay is performed by fluorescence spectrometry, luminescence spectrometry, fluorescence activated cell analysis, fluorescence activated cell sorting, automated microscopy or automated imaging.

12. (original) A method according to claim 1 whereby the assay is performed in live cells, in fixed cells, or in cell lysates.

13.(amended) A method according to claim 1 whereby the molecules fused to the protein reporter fragments ~~of the~~ used in said PCAs' are identified by a method chosen from the group consisting of: (a) cDNA library screening; (b) interaction mapping; and (c) prior knowledge of the existence of an interaction between a pair of proteins.

14. (original) A method according to claim 1 wherein the subcellular distribution of the assay signal and/or the intensity of the assay signal is determined.

15. (original) A method according to claim 5 wherein the reporter is a dihydrofolate reductase, a beta-lactamase, a luciferase, a green fluorescent protein, or a yellow fluorescent protein.

16.(amended) A method according to claims 1 wherein said chemical compounds are selected from the group consisting of synthetic molecules, known drugs, natural products, peptides, nucleic acids, antibodies, and small interfering RNAs.

17. (amended) Protein fragment complementation assays for drug discovery comprising a reassembly of separate fragments of a protein reporter molecule wherein reassembly of the protein reporter fragments generates an optically detectable signal with the proviso that said protein

fragments are not ubiquitin fragments and said assay is not a two hybrid assay.

18.(amended) Protein fragment complementation assays for drug discovery wherein the assay signal is detected with automated instrumentation with the proviso that said assays do not utilize ubiquitin fragments and said assays are not a two hybrid assay.

19.(amended) Assays according to claim 17 wherein the reporter molecule is selected from the group consisting of an enzyme, a fluorescent protein, a luminescent protein, ~~a phosphorescent protein,~~ a monomeric protein, an antigen, or an antibody.

20.(amended) Assays according to claim 17 or claim 18 wherein the assay signal is fluorescence, bioluminescence, chemiluminescence.~~, or phosphorescence.~~

21.(original) Assays according to claim 17 wherein said assays are performed in multiwell formats, in microtiter plates, in multispot formats, or in arrays.

22. (original) Assays according to claim 17 whereby said assays are performed by fluorescence spectrometry, luminescence spectrometry, fluorescence activated cell analysis, fluorescence activated cell sorting, automated microscopy or automated imaging.

23. (original) Assays according to claim 17 whereby said assays are performed in live cells, in fixed cells, or in cell lysates.

24. (original) Assays according to claim 17 wherein the subcellular distribution of the assay signal and/or the intensity of the assay signal is determined.

25. (original) Assays according to claim 17 wherein the reporter is a dihydrofolate reductase, a lactamase, a luciferase, a green fluorescent protein, or a yellow fluorescent protein.

26.(amended) An assay composition for drug discovery comprising complementary fragments of a first protein reporter molecule, said protein complementary fragments exhibiting a detectable activity when associated, wherein each fragment is fused to a separate molecule with the proviso that said protein fragments are not ubiquitin fragments and said assay is not a two hybrid assay.

27.(amended) An assay composition for drug discovery comprising a product selected from the group consisting of: (a) a first fusion product comprising: 1) a first fragment of a first protein reporter molecule whose fragments exhibit a detectable activity when associated and 2) a second molecule that is fused to said first protein fragment; (b) a second fusion product comprising 1) a second fragment of said first protein reporter molecule and 2) a third molecule that is fused to said second protein fragment; and c) both (a) and (b) with the proviso that said protein fragments are not ubiquitin fragments and wherein said fusion products (a) and (b) are not two hybrid constructs.

28.(canceled)

29.(amended) An assay composition for drug discovery comprising a nucleic acid molecule coding for a protein reporter fragment fusion product, which molecule comprises sequences coding for a product selected from the group consisting of: (a) a first protein reporter fusion product comprising: 1) fragments of a first protein reporter molecule whose fragments can exhibit a detectable activity when associated and 2) a second molecule fused to the fragment of the first molecule; (b) a second fusion product comprising 1) a second protein fragment of said first protein reporter molecule and 2) a second or third molecule; and (c) both (a) and (b) with the proviso that said protein fragments are not ubiquitin fragments and wherein said fusion products (a) and (b) are not two hybrid constructs.

30.(amended) An assay composition for drug discovery comprising a product selected from the group consisting of: (a) a first fusion product comprising: 1) a first protein fragment of a first protein reporter molecule whose fragments exhibit a detectable activity when associated and 2) a second molecule that is fused to said first protein fragment; (b) a second fusion product comprising 1) a second protein fragment of said first protein reporter molecule and 2) a third molecule that is fused to said second protein fragment; and (c) a third fusion product comprising: 1) a first protein fragment of a second protein reporter molecule whose fragments exhibit a detectable activity when associated and 2) a fourth molecule that is fused to said first protein fragment; (d) a fourth fusion product comprising 1) a second protein fragment of said second protein reporter molecule and 2) a fifth molecule that is fused to said second protein fragment; and e) a combination of (a), (b), (c) and (d) with the proviso that said protein fragments are not ubiquitin fragments and wherein said fusion products (a) and (b) are not two hybrid constructs.

31.(amended) An assay composition for drug discovery comprising a nucleic acid molecule coding for a protein reporter fragment fusion product, which molecule comprises sequences coding for a product selected from the group consisting of: (a) a first protein reporter fusion product comprising: 1) a fragments of a first protein reporter molecule whose fragments can exhibit a detectable activity when associated and 2) a second molecule fused to the protein fragment of the first protein reporter molecule; (b) a second fusion product comprising 1) a fragments of a second protein reporter molecule whose fragments can exhibit a detectable activity when associated and 2) a third molecule fused to the protein fragment of the second protein reporter molecule; and (c) both (a) and (b) with the proviso that said protein fragments are not ubiquitin fragments and wherein said fusion products (a) and (b) are not two hybrid constructs.

32.(amended) An assay composition for drug discovery comprising an expression vector comprising a polynucleotide encoding ~~containing~~ at least one molecule of interest that is operably linked to a protein reporter fragment.

33.(amended) An assay composition for drug discovery comprising an expression vector comprising a polynucleotide encoding ~~containing~~ (a) a constitutive or an inducible promoter and (b) a gene of interest operably linked to a protein reporter fragment.

34.(amended) An assay composition for drug discovery comprising at least one expression vector comprising a polynucleotide encoding ~~containing~~ (a) a first molecule of interest that is operably linked to a protein fragment of a first protein reporter, and (b) a second molecule that is

operably linked to a protein fragment of a second protein reporter.

35.(amended) An assay composition according to ~~any one of~~ claim 26 wherein one or more reporter fragment(s) are derived from the group consisting of a fluorescent protein, a bioluminescent protein, a chemiluminescent protein, ~~a phosphorescent protein,~~ an enzyme, a monomeric protein, an antibody and an antigen.

36.(amended) A method, assay or composition according to any one of claims 1, 17, or 26 wherein at least one of the molecules fused to a protein reporter fragment is selected from the group consisting of a receptor, a tumor suppressor gene, a kinase, a kinase substrate, an oncogene, an adaptor protein, a ubiquitin-like molecule, and a transcription factor.

37.(amended) A method, assay or composition according to any one of claims 1, 17 or 26 wherein at least one of the molecules fused to a protein reporter fragment is selected from the group consisting of p53, Chk1, ATR, ATM, Rad 51, PDK2, STAT1, FKBP, FRAP, p70S6Kinase, S6 protein, 4E-BP1, PPP2A, TNFR, TRADD, FADD, p65 subunit of NFkappaB, p50 subunit of NFkappaB, CBP, TRAF2, Ubiquitin, IKK-beta, IKK-gamma, IkappaBalpha, MEK, ERK, PI-3-Kinase, PKB, Ft1, GCN4, PDK1, GSK3, NF-AT, and Calcineurin; and domains, fragments or homologues thereof.

38.(original) A method according to claim 2 wherein the pathway is a DNA damage response pathway, a receptor tyrosine kinase pathway, a cytokine-dependent pathway, a nutrient-

activated pathway, a proteasome pathway, a growth factor-dependent pathway, a mitogen-activated pathway, a hormone-dependent pathway, a heat shock protein pathway, a ubiquitin pathway, a cell cycle pathway, a T-cell pathway or an apoptotic pathway.

39.(original) A method, assay or composition according to any one of claims 1, 17, or 26 whereby the assay is used to screen for a receptor agonist, a receptor antagonist, a kinase inhibitor, a phosphatase inhibitor, a cell cycle inhibitor, a heat shock protein inhibitor, an E3 ligase inhibitor, a transcription factor inhibitor, an inhibitor of a protein-protein interaction, or a proteasome inhibitor.